**Angiotensin-Converting Enzyme (ACE) Inhibitors**

ACE inhibitors competitively inhibit ACE, which converts angiotensin I to angiotensin II. This blunts the increase in systemic vascular resistance, adverse cardiac remodeling and hypertrophy effects, and aldosterone release caused by angiotensin II. ACE inhibitors are modest balanced vasodilators. They may reduce systemic vascular resistance up to 25%, improving cardiac output and reducing regurgitant fraction in mitral regurgitation. Additional benefits include a reduction in left ventricular filling pressures and thus pulmonary venous congestion. It is thought that the beneficial effects of ACE inhibitors are primarily due to neurohormonal modulation, in addition to hemodynamic benefits. Studies in dogs with CHF have demonstrated improved clinical scores when an ACE inhibitor was added to standard therapy (diuretics with or without digitalis glycoside), with more dramatic improvements generally seen in dogs with DCM than in those with CVD. A trend toward prolonged survival was also seen in some studies.

In general, cardiologists agree that an ACE inhibitor is indicated in CHF. The benefit of ACE inhibitor therapy before the onset of CHF is more controversial and should be based on the individual patient and underlying disease. It may be appropriate to initiate therapy in any dog with clearly depressed systolic function (ie, occult DCM) in hopes of delaying ongoing remodeling, or in dogs with CVD and documented hypertension (systemic blood pressure >160 mm Hg), but there are no well controlled studies to support this claim. Studies of ACE inhibition in cats are limited, and none has shown a true statistical benefit to ACE inhibition beyond what is gained from standard diuretic therapy in cats with CHF. Furthermore, no benefit has been shown in delaying the progression of occult HCM. These studies have low patient numbers, however, and most cardiologists do prescribe an ACE inhibitor in addition to appropriate background therapy for cats in CHF.

Adverse effects of ACE inhibition are generally related to a reduced glomerular filtration rate (GFR) in hypovolemia or preexisting renal insufficiency, as angiotensin II promotes renal efferent arteriolar constriction in the face of reduced renal perfusion. Most commonly, adverse effects are noted in animals with azotemia related to poor cardiac output, overzealous diuretic administration, or preexisting renal insufficiency. Anorexia, vomiting, and lethargy may occur. Although cough is a common adverse effect of ACE inhibitor therapy in people, this is not seen in dogs and cats. Some animals may develop transient azotemia or hyperkalemia after starting ACE inhibitor therapy. For this reason, it is recommended that renal values and electrolytes be checked before starting an ACE inhibitor and 5–7 days later.

Enalapril is the only approved ACE inhibitor in the USA for dogs with CHF. It is generally started at 0.5 mg/kg, PO, sid or 0.25 mg/kg, bid in dogs with mild heart failure; dosage may subsequently be increased to 0.5 mg/kg, bid in dogs with moderate to severe heart failure. Longterm dosing in cats is recommended at 0.5 mg/kg, PO, sid. Clinical benefits are not commonly seen before 2–3 wk. Renal values should be monitored periodically (at least every 6 mo) while on longterm ACE inhibitor therapy.

Other ACE inhibitors used for the treatment of heart failure include benazepril (0.25–0.5 mg/kg, PO, sid-bid), captopril (0.5–2.0 mg/kg, PO, bid-tid), and lisinopril (0.5 mg/kg, PO, sid-bid). Unlike enalapril and other ACE inhibitors that are renally excreted, benazepril undergoes significant hepatobiliary elimination (up to 50% in dogs and 85% in cats). Whether benazepril is safer or more effective in patients with renal insufficiency remains to be seen.

SOURCE: http://www.merckmanuals.com/vet/circulatory\_system/heart\_disease\_and\_heart\_failure/heart\_failure.html